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EXAMINER

TSAY, MARSHA M

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/593,213	<b>Applicant(s)</b> LOTZ ET AL.	
	<b>Examiner</b> Marsha M. Tsay	<b>Art Unit</b> 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 April 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-38 is/are pending in the application.
- 4a) Of the above claim(s) 1-21 and 25-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>09/15/06</u> .  | 6) <input type="checkbox"/> Other: _____                          |

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Applicant's election with traverse of group (1), i.e. nucleic acid, vector, host cell, and protein, in the reply filed August 5, 2009, is acknowledged. The traversal is on the ground(s) that the nucleic acids according to group (1) and antisense nucleic acids according group (2) derive from each other and they can both be used in a method according to claim 22 in the same way. For example, both types of nucleic acids can be used in a method using a DNA array. Furthermore, both of these nucleic acid molecules are parts of the same double-stranded DNA molecule as used in, for example, a vector. Therefore, the restriction between group (1) and group (2) should be withdrawn. Applicants' remarks are not persuasive regarding having the restriction between groups (1) and (2) withdrawn. Firstly, it should be noted that the complementary strand of 22(d) is part of the same double-stranded DNA as the nucleic acid of 22(a) to 22(c), and is included in group (1). However, the nucleic acid of 22(e) may be structurally and functionally different than the complementary strand, i.e. it has to inhibit the expression of a cell wall protein of a pathogenic fungal organism in antisense orientation to a promoter in a host cell. Therefore, having antisense orientation to a promoter would not mean that the nucleic acid of 22(e) is part of the same double-stranded DNA molecule as the nucleic acid of 22(a) to 22(c). Therefore, the restriction between groups (1), (2), and (3) is maintained and made final because each of the molecules of groups (2) and (3) are chemically, functionally, and structurally different than the molecules of group (1). Moreover, the technical feature is not a contribution over the prior art for at least the reasons set forth in the rejection under 35 U.S.C. 103(a) below.

Claims 1-21, 25-38 have been withdrawn from further consideration by the Examiner because they are drawn to non-elected inventions. Claims 22-24, to nucleic acids (sense and

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complementary strands), vector, host cell, and protein, and SEQ ID NOS. 1/2, are currently under examination.

Priority: The request for priority to GERMANY 10 2004 013 826.5, filed March 16, 2004, is acknowledged. A certified copy of the foreign priority document has been filed in this case on 9/15/06 and is in a non-English language.

### ***Specification***

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code: specification p. 61-62. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

### ***Claim Objections***

Claim 22 is objected to because of the following informalities: claim 22 is objected because it recites non-elected inventions, *e.g.*, an antibody. Further, in claim 22, it is unclear if the letter (e) is referring to just antisense nucleic acid or if it also includes vector, host cell, a protein and an antibody. Further clarification regarding claim 22(e) is requested. It appears as if the “a nucleic acid molecule which encodes a cell wall protein...” should be labeled as, *e.g.*, “1)” and vector, host cell, protein, and antibody labeled as 2), 3), 4), and 5), respectively. Appropriate correction is required.

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***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method for the discovery and identification of substances having therapeutic action against diseases which are caused by *Candida* species or pathogenic fungal *Trichosporon*, wherein a substance to be tested is brought into contact in a suitable medium with at least one agent and an interaction between the substance to be tested and the agent is detected (claim 22), and compositions comprising an agent identified by said method (claims 23-24). *Vas-Cath Inc. V. Mahurkar*, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” As stated above, the discovery and identification of substances having therapeutic action against diseases which are caused by *Candida* species or pathogenic fungal *Trichosporon* (claim 22). It is noted that claim 22 requires “an interaction between the substance to be tested and the agent is detected”,

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*i.e.*, the claim requires a positive indication of detecting an interaction between the test substance and the recited agent, where the substance is described in the preamble as “having therapeutic action against diseases...” Claims 23-24 are drawn to “an agent” identified according to claim 22. The specification does not disclose any correlation between the recited agents and the structure of any substance(s) that would have therapeutic action against diseases caused by *Candida* and pathogenic *Trichosporon*. The specification appears to describe a method of screening for substances that are regulated by Rim101p; however, the substances identified by screening appear to be SEQ ID NOS: 1 and 2, *i.e.* *Candida albicans* cell wall protein Rbr1p. The specification does not appear to disclose any substances that were identified by an *interaction* between the agents of SEQ ID NO: 1 and/or 2 and have the activity of therapeutic action against diseases caused by *Candida* and pathogenic *Trichosporon*. Therefore, one of ordinary skill would conclude that Applicants would not have been in possession of the claimed method for the discovery and identification of substances having therapeutic action against diseases which are caused by *Candida* and pathogenic *Trichosporon* (claim 22) or the “agents” identified according to said method (claims 23-24).

Additionally, claims 22(c) and 22(d) recite nucleotide sequences which have a homology of at least 80% to the nucleotides of 22(a) and 22(b) and a nucleotide sequence that is complementary to the nucleotides of 22(a) to 22(c), respectively, where the nucleic acids have the “function” of encoding a cell wall protein necessary for the hyphae development of a pathogenic fungal organism. It is noted that the nucleic acid of claim 22(d) is not required to be complementary over the full length of the nucleic acid of a) to c) and can be partially complementary. Also, it is noted that the “vector” of claim 22 “contains a nucleic acid

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molecule”, but is not required to contain any of the nucleic acids of a) to d). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” As stated above, the discovery and identification of substances having therapeutic action against diseases which are caused by *Candida* species or pathogenic fungal *Trichosporon* (claim 22). It is noted that claim 22 requires “an interaction between the substance to be tested and the agent is detected”, *i.e.*, the claim requires a positive indication of detecting an interaction between the test substance and the recited agent, where the substance is described in the preamble as “having therapeutic action against diseases...” One of ordinary skill cannot necessarily envision the detailed structures of ALL of the derivatives of SEQ ID NO: 1 (nucleic acid sequence) or the derivatives of nucleotides encoding SEQ ID NO: 2 (amino acid sequence) because nowhere in the specification is it described which regions of SEQ ID NOS: 1/2 are required for the activity of being a cell wall protein necessary for the hyphae development of a pathogenic fungal organism. Therefore, one of ordinary skill would conclude that Applicants would not have been in possession of the claimed method for the discovery and identification of substances having therapeutic action against diseases which are caused by *Candida* and pathogenic *Trichosporon* (claim 22) or the “agents” identified according to said method (claims 23-24).

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method acquiring it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

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Claims 22-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method using SEQ ID NO:1, the full-length complement of SEQ ID NO:1, or SEQ ID NO:2 (claim 22) or a composition comprising a polynucleotide encoding SEQ ID NO:2 or a the polypeptide of SEQ ID NO:2 (claims 23-24), does not reasonably provide enablement for methods using all "agents" and all diagnostic and pharmaceutical compositions as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As stated above, claim 22 is drawn to a method for the discovery and identification of substances having therapeutic action against diseases which are caused by *Candida* species or pathogenic fungal *Trichosporon* using (in relevant part) a nucleic acid comprising any partial complement of the nucleic acids of a) to c) and a vector containing any nucleic acid molecule. The diagnostic and pharmaceutical compositions of claims 23-24 encompass *any* agent identified by the method of claim 22.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by



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weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In this case, the specification discloses only three working examples of "agents" as encompassed by the claims, *i.e.*, SEQ ID NO:1, the full-length complement of SEQ ID NO:1, or SEQ ID NO:2. Other than SEQ ID NO:1, the full-length complement of SEQ ID NO:1, or SEQ ID NO:2, the specification fails to provide even a single working example of a diagnostic "agent" identified by the method of claim 22. The specification fails to provide even a single working example of a pharmaceutical "agent" identified by the method of claim 22. Moreover, the specification fails to provide any guidance for using a vector comprising any nucleic acid as a detection or diagnostic agent and further fails to provide any guidance for using any agent identified by the method of claim 22 for a pharmaceutical use. The state of the prior art is such that many agents are available for screening and/or diagnostic or therapeutic use, however, without sufficient guidance, it would require undue experimentation to identify and use all agents as broadly encompassed by the claims.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claim is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is drawn to a method for the discovery and identification of substances having therapeutic action against diseases caused by *Candida* species or pathogenic fungal *Trichosporon*. Claim 22 lines 3-5 recite "wherein a substance to be tested is brought into contact in a suitable medium with at least one agent and an interaction between the substance to be tested and the agent is detected." It is unclear what the interaction is and/or how the interaction is to be tested and/or detected. Further clarification is requested.

Further claim 22 recites a nucleic acid molecule which encodes a cell wall protein...and which is selected from the group consisting of (a) to (e), a vector, a host cell, a protein, and an antibody. However, the nucleic acid of part (d) would be a complementary, non-coding strand of SEQ ID NO: 1, i.e. the complement of SEQ ID NO: 1 would not be expected to encode a cell wall protein. It should be noted that a cell, a protein, and an antibody are not nucleic acids. Therefore, it does not make sense to include these components under claim 22(e).

Further, claims 23-24 are drawn to an agent identified according to the method of claim 22. It should be noted that claim 22 recites identification of a "substance" and not an "agent." The "agent" recited in claim 22 is referring to a nucleic acid molecule selected from the group consisting of elected SEQ ID NOS: 1 and 2. Therefore, claims 23-24 need to be clarified in regards to whether the diagnostic composition comprises "an agent" or "a substance" (claim 23)

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and whether the pharmaceutical composition comprises "an agent" or "a substance" (claim 24).

Further clarification is requested.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 22-24 are rejected under 35 U.S.C. 102(a) as being anticipated by Lotz et al. (2004 Eukaryotic Cell 3(3): 776-784). For examination purposes, the preamble phrase "...for the discovery and identification...*Blastochizomyces* species..." in claim 22 is interpreted as an intended use of the method and is accorded no patentable weight. Claim 22 is interpreted as a method of identifying a substance comprising bringing said substance into contact with at least one agent, detecting an interaction between said substance and the at least one agent, and wherein the agent is selected from the group consisting of a nucleic acid selected from part (a) to part (d).

Lotz et al. teach a method comprising using DNA microarray analysis to identify RIM101-regulated cell wall genes in *C. albicans* (p. 778, columns 1-2). The method of Lotz uses a DNA microarray comprising orf6.647 to measure the amount of hybridizing orf6.647 mRNA in wild-type *C. albicans* and a mutant *C. albicans* RIM101 knockout (p. 777, column 2). On pages 10 and 60 of the instant specification, SEQ ID NO:1 and 2 are alternatively referred to as Rbr1p, Rbr1, and orf6.6747. This anticipates claims 22-24 as written.

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Should Applicant present an argument that the reference of Lotz et al. cannot be applied in a rejection under 35 U.S.C. 102(a) due to the date of the publication, Applicant should provide an English translation of the priority document submitted with the instant application.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sohn et al. (2003 Molecular Microbiology 47(1): 89-102; IDS 09.15.06) in view of Tsong et al. (2003 Cell 115(4): 389-399; pdf copy is provided) and as evidenced by Lotz et al. (2004 Eukaryotic Cell 3(3): 776-784). Sohn et al. disclose a method of screening for novel genes transcribed differentially during the yeast-to-hyphae transition comprising using DNA microarray comprising 117 probes that represent 35 known as well as 75 not further characterized open reading frames (ORFs) of *C. albicans* (p. 89-90). Although Sohn et al. does not expressly teach their DNA microarray comprises orf6.6747 (on page 60 of the instant specification, Rbr1 is also identified as orf6.6747), evidentiary reference Lotz et al. teaches a nucleic acid array comprising orf6.6747 (see, e.g., p. 778, Table 3), noting that this array has already been described by Sohn et al. (p. 777, column 2, middle and p. 778, column 1, bottom). Sohn et al. does not teach detecting an interaction between orf6.6747 and “a substance to be tested”.

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Tsong et al. disclose a table of *C. Albicans* genes that were identified by microarray analysis (p. 14 of pdf copy), including orf6.6747 (p. 62 of pdf copy).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Sohn et al. to measure the amount of orf6.647 mRNA. The motivation to do so is given by Sohn et al. which disclose that a method of screening for novel genes can be performed using DNA microarray comprising ORFs of *C. albicans* and since Tsong et al. disclose a table of ORFs of *C. albicans*, including instant orf6.6747 (Rbr1), one of ordinary skill would expect to be successful in screening for the level of orf6.647 mRNA because Sohn et al. inherently teaches and Tsong et al. explicitly teaches DNA arrays with orf6.647, which can be used for DNA microarray screening using ORFs of *C. albicans*.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

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applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

August 27, 2009

/David J. Steadman/  
Primary Examiner, Art Unit 1656